Chapter 3

Asthma Genomics: Implications for Public Health

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What Causes Asthma?

Asthma is a chronic lung condition characterized by airway inflammation, airway hyper-reactivity and reversible airway obstruction. The disease is found disproportionately in children and minorities, and prevalence has increased significantly since the early 1980s. No single factor is responsible for the development of asthma. Environmental exposures, such as house dust mites, fungal spores, cockroaches, tobacco smoke, and animal dander have been identified as contributors. In addition, as early as the 1920s, studies demonstrated the existence of a familial predisposition to asthma. There is strong evidence for both genetic and environmental contributors to the development of asthma.

Public Health Implications of Asthma Genomics Research

In 2003, the Asthma Working Group, created by the University of Washington Center for Genomics and Public Health, organized an evaluation of the implications of asthma genomics research for public health. Based on an initial literature review and discussion, the UW Asthma Working Group identified four areas of potential action in which genomic research or information might contribute to public health efforts to reduce asthma morbidity and mortality:

- population-based prevention,
- targeted prevention based on risk status,
- diagnosis, and
- management.

The Working Group also defined five key perspectives to use when evaluating potential interventions:

- patient and family,
- community,
- researcher,
- health care professional, and
- public health practitioner.

The plan for expert consultation sought feedback on these potential areas of intervention and important considerations from each of the identified perspectives. A sixth perspective—that of the commercial developer—was added based on comments made during the consultation.

The first round of consultation made use of asthma expertise available in the Seattle community and in Washington State. Subsequent rounds of consultation sought advice from:

- experts at the University of Michigan Center for Genomics and Public Health and the University of North Carolina Center for Genomics and Public Health,
- national experts identified through consultation with local and federal advisors, and
- experts attending the American Thoracic Society meeting (Seattle, May 2003) and the National Conference on Asthma 2003 (Washington DC, June 2003).

Experts were interviewed individually or in small groups; most experts also identified additional relevant medical literature. Over the course of the consultation and literature review, some common themes emerged. These included the potential role of **genomic profiling** as a means for identifying individuals with increased asthma risk; the implications of commercial incentives for technology development; the relevance of current data on behavioral interventions, treatment adherence and clinical outcomes for potential genome-based interventions; and the significance of current data related to differences in asthma prevalence across demographic groups for public health research and actions.

Genomic Profiling
Concurrent detection of multiple gene variants associated with predisposition to a particular disease.

Pharmacogenomics and Predictive Testing

Pharmacogenomics
Refers to the use of genomic techniques to enhance drug development and define drug responses.

Consultants consistently identified **pharmacogenomics** as the area of genomic research most likely to change asthma care in the near future. Genetic factors have been estimated to account for 60% to 80% of the variability in asthmatics patients' response to medications.[1] Genomic strategies will aid in the identification of new drug targets, and may lead to drugs designed for use in specific subsets of

asthmatic patients, defined by genotype. In addition, pharmacogenomic research will produce genetic tests designed to predict drug responses and adverse side effects.

In the long term, genomic research may also produce genetic tests that will aid in disease classification, predict prognosis, or identify unaffected children who are at increased risk to develop asthma. One possible application of the latter capability would be newborn testing, to identify infants who might benefit from environmental modifications or immunotherapy for prevention. While such research holds promise for innovative treatments and effective prevention, it will not succeed without careful attention to the interaction between genetic and non-genetic contributors to asthma.

Public Health Actions—Asthma Genomics Research

Actions on the part of public health can help to ensure that genomic research supports public health goals to reduce asthma morbidity and mortality. These include:

- On-going critical evaluation of research on genetic contributors to asthma, to guard against overly simplistic interpretation of data addressing genetic hypotheses. Headlines proclaim the discovery of "the gene for disease X", without much attention to the complex etiology of diseases such as asthma.[2] Researchers and practitioners concerned about the public health implications of asthma research need to be vigilant against the over-interpretation of genetic data, or an overly ready assumption of genetic causes for observed differences.

- Funding and advocacy, to ensure that evidence gaps are addressed with appropriate research strategies. In particular, public health input will help to ensure adequate selection and definition of study populations, meaningful measures of environmental exposure, and inclusion of appropriate clinical outcomes.

- Participation in design of recruitment and data management strategies for population-based genomic research. CDC and state public health agencies could play an important role in crafting public messages and recruitment strategies to ensure adequate participation in population-based studies, and in developing policies for data collection and management that reduce fears about inappropriate uses of genetic information.

- Support for evidence-based practice in pharmacogenomics and genetic testing, including rigorous assessment of the utility and cost-effectiveness

of drugs requiring prior testing to determine candidacy for treatment, and of genetic tests proposed as a means to tailor drug regimens or predict future disease.[3]

- Advocacy to ensure access to genomics-based therapies for the medically underserved, when they are found to be cost-effective.

- Utilization of the convening power of public health, to foster multidisciplinary collaboration in research and broad stakeholder participation in the development of research and clinical practice policies.

In order to accomplish these goals, public health will need an infrastructure for technical support, consultation, and education. The most efficient approach is likely to involve an incremental development of expertise, starting with a small, centralized, multidisciplinary group that works in partnership with designated state liaison persons and academic centers conducting research in public health genetics.

References

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